

We claim:

1. A method for treating a patient, who is to receive a cytotoxic agent, which comprises the steps of:
 - (a) determining the circulating suramin concentration in said patient;
 - (b) administering suramin, if required, in a required dose to establish a low circulating concentration of suramin in said patient of below about 200 μM ; and
 - (c) administering said cytotoxic agent to said patient when said low circulating concentration of suramin of below about 200 μM is present in said patient.
2. The method of claim 1, wherein said low dose of circulating suramin is between about 10 and 200 μM .
3. The method of claim 2, wherein said low dose of circulating suramin is between about 10 and 50 μM .
4. The method of claim 1, wherein the required dose of suramin can be determined in step (b) by the steps of:
 - (b1) determining the gender and the squared value of the body surface area (BSA) of said patient;
 - (b2) determining the time elapsed, in days, since the initiation of the last suramin treatment; and
 - (b3) calculating the dose of low dose suramin using a nomogram that shows the dose according to the parameters of gender, squared value of body surface, and elapsed days since last suramin treatment.
5. The method of claim 4, wherein said nomogram comprises:

Nomogram For Calculating Suramin Dose

| FACTOR | |
|--------|-------|
| Man | Woman |

| Cycle 1* | 125 | 125 |
|--|--------|-----|
| Days since the administration of the first dose of previous cycle | FACTOR | |
| 7 | 39 | 33 |
| 8 | 43 | 37 |
| 9 | 47 | 40 |
| 10 | 51 | 44 |
| 11 | 55 | 47 |
| 12 | 58 | 50 |
| 13 | 61 | 53 |
| 14 | 64 | 56 |
| 15 | 67 | 58 |
| 16 | 70 | 61 |
| 17 | 72 | 63 |
| 18 | 74 | 66 |
| 19 | 77 | 68 |
| 20 | 79 | 70 |
| 21 | 80 | 72 |
| 22 | 82 | 74 |
| 23 | 84 | 75 |
| 24 | 86 | 77 |
| 25 | 87 | 79 |
| 26 | 88 | 80 |
| 27 | 90 | 82 |
| 28 | 91 | 83 |
| 29 | 92 | 84 |
| 30 | 93 | 86 |
| 31 | 94 | 87 |
| 32 | 95 | 88 |
| 33 | 96 | 89 |
| 34 | 97 | 90 |
| 35 | 98 | 91 |
| 36 | 98 | 92 |
| 37 | 99 | 93 |
| 38 | 100 | 94 |
| 39 | 100 | 95 |
| 41 | 102 | 96 |
| 42 | 102 | 97 |
| 44 | 103 | 98 |
| 47 | 104 | 100 |
| 49 | 105 | 101 |
| 52 | 106 | 102 |
| 55 | 106 | 103 |

where:

$$\text{First cycle dose (mg)} = \frac{(21.4 * 5.13 * \text{BSA}^2)}{e^{-(0.0026 \text{ or } 0.0022 * 48)}} = \text{FACTOR} * \text{BSA}^2 \quad \text{Eq. 15}$$

and

5

$$\text{Subsequent cycle dose} = \text{First dose} * (1 - e^{-k * t}) = 125 * \text{BSA}^2 * (1 - e^{-k * t}) \quad \text{Eq. 16.}$$

6. The method of claim 1, wherein said cytotoxic agent is one or more of an anti-microtubule agent, a topoisomerase I inhibitor, a topoisomerase II inhibitor, an anti-metabolite, a mitotic inhibitor, an alkylating agent, an intercalating agent, an agent capable of interfering with a signal transduction pathway, an agent that promotes one or more of apoptosis or necrosis, an interferon, an interleukin, a tumor necrosis factor, or radiation.

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15 7. The method of claim 6, wherein said cytotoxic agent is one or more of paclitaxel, vincristine, vinblastine, vindesine, vinorelbin, docetaxel, topotecan, camptothecin, irinotecan hydrochloride, doxorubicin, etoposide, mitoxantrone, daunorubicin, idarubicin, teniposide, amsacrine, epirubicin, merbarone, piroxantrone hydrochloride, 5-fluorouracil, methotrexate, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, cytosine arabinoside, trimetrexate, gemcitabine, acivicin, alanosine, pyrazofurin, N-Phosphoracetyl-L-Asparate (PALA), pentostatin, 20 5-azacitidine, 5-Aza-2'-deoxycytidine, adenosine arabinoside, cladribine, ftorafur, UFT (combination of uracil and ftorafur), 5-fluoro-2'-deoxyuridine, 5'-deoxy-5-fluorouridine, tiazofurin, Xeloda (Capecitabine), cisplatin, carboplatin, oxaliplatin, mitomycin C, BCNU, melphalan, thiotepa, busulfan, chlorambucil, plicamycin, dacarbazine, ifosfamide phosphate, cyclophosphamide, nitrogen mustard, uracil mustard, pipobroman, 4-ipomeanol, dihydrolenperone, spiromustine, geldanamycins, cytochalasins, depsipeptide, leuprolide (e.g., Lupron), ketoconazole, tamoxifen, goserelin, flutamide, 4'-cyano-3-(4- fluorophenylsulphonyl)-2-hydroxy-2-methyl-3'-(trifluoromethyl) propionanilide, 30 Herceptin, anti-CD20 (Rituxan), C225, Iressa, interferon alpha, interferon beta,

interferon gamma, interleukin 2, interleukin 4, interleukin 12, tumor necrosis factors, radiation, hydroxyurea, azathioprine, aminopterin, trimethoprin, pyrimethamine, pyritrexim, DDMP (2,4 diamino- 5(3',4' dichlorophenyl)6 methylpyrimidine), 5,10-dideazatetrahydrofolate,10-propargyl-5,8 dideazafolate (CB3717), 10-ethyl-10-deaza-aminopterin, deoxycytidine, 5-aza-cytosine arabinoside, N-4-palmitoyl-ara C, 2'-azido-2'-deoxy-ara C, N4-behenoyl-ara C, CCNU (lomustine), estramustine, MeCCNU, triethylene melamine, trenimon, dimethyl busulfan, streptozotocin, chlorozotocin, procarbazine, hexamethylmelamine (Altretamine), pentamethylmelamine (PMM), tetraplatin, oxaliplatin, platinum-DACH, aziridinybenzoquinone (AZQ), bleomycin, tallysomyacin S₁₀^b, liblomycin, pepleomycin, asparaginase (Elspar), pegaspargase (Oncaspar), Cladribine (leustatin), porfimer sodium (Photofrin), amonofide, deoxyspergualin, dihydrolenperone, flavone acetic acid, gallium nitrate, or hexamethylene bisacetamine (HMBA).

8. The method of claim 1, wherein a suramin dose is administered such that a concentration of between about 10 to about 50 μ M over 48 hours is achieved in a patient.

9. The method of claim 1, wherein the patient is a mammal.

10. The method of claim 9, wherein the patient is a human.

11. The method of claim 1, wherein the patient has a tumor.

12. The method of claim 7, wherein the cytotoxic agent is one or more of carboplatin or paclitaxel.

13. The method of claim 1, wherein two-thirds of the therapeutically effective amount of suramin is given on the first day and the remaining one-third of the therapeutically effective amount of suramin is given about 24 hours later.

14. The method of claim 1, wherein the required dose of suramin can be determined in step (b) by the steps of:

- (b1) determining the squared value of the body surface area (BSA) of said patient;
- (b2) determining the time elapsed, in days, since the initiation of the last suramin treatment; and
- (b3) calculating the dose of low dose suramin using a nomogram that shows the dose according to the parameters of gender, squared value of body surface, and elapsed days since last suramin treatment.

15. The method of claim 14, wherein said nomogram comprises:

Nomogram For Calculating Suramin Dose

| Cycle 1* | 125 |
|---|--------|
| Days since the administration of the first dose of previous cycle | FACTOR |
| 7 | 39 |
| 8 | 43 |
| 9 | 47 |
| 10 | 51 |
| 11 | 55 |
| 12 | 58 |
| 13 | 61 |
| 14 | 64 |
| 15 | 67 |
| 16 | 69 |
| 17 | 72 |
| 18 | 74 |
| 19 | 76 |
| 20 | 78 |
| 21 | 80 |
| 22 | 82 |

| | |
|----|-----|
| 23 | 84 |
| 24 | 86 |
| 25 | 87 |
| 26 | 88 |
| 27 | 90 |
| 28 | 91 |
| 29 | 92 |
| 30 | 93 |
| 31 | 94 |
| 32 | 95 |
| 33 | 96 |
| 34 | 97 |
| 35 | 98 |
| 36 | 98 |
| 37 | 99 |
| 38 | 100 |
| 39 | 100 |
| 41 | 102 |
| 42 | 102 |
| 44 | 103 |
| 47 | 104 |
| 49 | 105 |
| 52 | 106 |
| 55 | 106 |

where:

$$\text{First cycle dose (mg)} = \frac{(21.4 * 5.13 * \text{BSA}^2)}{e^{-(0.0026 \text{ or } 0.0022 * 48)}} = \text{FACTOR} * \text{BSA}^2 \quad \text{Eq. 15}$$

and

5

$$\text{Subsequent cycle dose} = \text{First dose} * (1 - e^{-k * t}) = 125 * \text{BSA}^2 * (1 - e^{-k * t}) \quad \text{Eq. 16.}$$

16. A method for determining a therapeutically effective amount of suramin for administering to a patient, who is to receive a cytotoxic agent, which comprises the steps of:

- 5 (a) determining the gender and the squared value of the body surface area (BSA) of said patient;
- (b) determining the time elapsed, in days, since the initiation of the last suramin treatment; and
- 10 (c) calculating the dose of low dose suramin using a nomogram that shows the dose according to the parameters of gender, squared value of body surface, and elapsed days since last suramin treatment.

17. The method of claim 16 wherein said nomogram comprises:

Nomogram For Calculating Suramin Dose

| | FACTOR | |
|---|--------|-------|
| | Man | Woman |
| Cycle 1* | 125 | 125 |
| Days since the administration of the first dose of previous cycle | FACTOR | |
| 7 | 39 | 33 |
| 8 | 43 | 37 |
| 9 | 47 | 40 |
| 10 | 51 | 44 |
| 11 | 55 | 47 |
| 12 | 58 | 50 |
| 13 | 61 | 53 |
| 14 | 64 | 56 |
| 15 | 67 | 58 |
| 16 | 70 | 61 |
| 17 | 72 | 63 |
| 18 | 74 | 66 |
| 19 | 77 | 68 |
| 20 | 79 | 70 |
| 21 | 80 | 72 |
| 22 | 82 | 74 |
| 23 | 84 | 75 |
| 24 | 86 | 77 |
| 25 | 87 | 79 |
| 26 | 88 | 80 |
| 27 | 90 | 82 |
| 28 | 91 | 83 |
| 29 | 92 | 84 |
| 30 | 93 | 86 |
| 31 | 94 | 87 |
| 32 | 95 | 88 |
| 33 | 96 | 89 |
| 34 | 97 | 90 |
| 35 | 98 | 91 |
| 36 | 98 | 92 |
| 37 | 99 | 93 |
| 38 | 100 | 94 |
| 39 | 100 | 95 |
| 41 | 102 | 96 |

| | | |
|----|-----|-----|
| 42 | 102 | 97 |
| 44 | 103 | 98 |
| 47 | 104 | 100 |
| 49 | 105 | 101 |
| 52 | 106 | 102 |
| 55 | 106 | 103 |

where:

$$\text{First cycle dose (mg)} = \frac{(21.4 * 5.13 * \text{BSA}^2)}{e^{-(0.0026 \text{ or } 0.0022 * 48)}} = \text{FACTOR} * \text{BSA}^2 \quad \text{Eq. 15,}$$

5 and

$$\text{Subsequent cycle dose} = \text{First dose} * (1 - e^{-k * t}) = 125 * \text{BSA}^2 * (1 - e^{-k * t}) \quad \text{Eq. 16.}$$

18. The method of claim 16, wherein said cytotoxic agent is one or more of an anti-
 10 microtubule agent, a topoisomerase I inhibitor, a topoisomerase II inhibitor, an anti-metabolite, a mitotic inhibitor, an alkylating agent, an intercalating agent, an agent capable of interfering with a signal transduction pathway, an agent that promotes one or more of apoptosis or necrosis, an interferon, an interleukin, a tumor necrosis factor, or radiation.

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19. The method of claim 18, wherein said cytotoxic agent is one or more of
 paclitaxel, vincristine, vinblastine, vindesine, vinorelbin, docetaxel, topotecan,
 camptothecin, irinotecan hydrochloride, doxorubicin, etoposide, mitoxantrone,
 daunorubicin, idarubicin, teniposide, amsacrine, epirubicin, merbarone,
 20 piroxantrone hydrochloride, 5-fluorouracil, methotrexate, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, cytosine arabinoside, trimetrexate, gemcitabine, acivicin, alanosine, pyrazofurin, N-Phosphoracetyl-L-Asparate (PALA), pentostatin, 5-azacitidine, 5-Aza-2'-deoxycytidine, adenosine arabinoside, cladribine, fltorafur, UFT (combination of uracil and fltorafur), 5-
 25 fluoro-2'-deoxyuridine, 5'-deoxy-5-fluorouridine, tiazofurin, Xeloda (Capecitabine), cisplatin, carboplatin, oxaliplatin, mitomycin C, BCNU, melphalan, thiotepa, busulfan, chlorambucil, plicamycin, dacarbazine, ifosfamide

phosphate, cyclophosphamide, nitrogen mustard, uracil mustard, pipobroman, 4-ipomeanol, dihydrolenperone, spiromustine, geldanamycins, cytochalasins, depsipeptide, leuprolide (e.g., Lupron), ketoconazole, tamoxifen, goserelin, flutamide, 4'-cyano-3-(4-fluorophenylsulphonyl)-2-hydroxy-2-methyl-3'-(trifluoromethyl) propionanilide, Herceptin, anti-CD20 (Rituxan), C225, Iressa, interferon alpha, interferon beta, interferon gamma, interleukin 2, interleukin 4, interleukin 12, tumor necrosis factors, radiation, hydroxyurea, azathioprine, aminopterin, trimethoprin, pyrimethamine, pyritrexim, DDMP (2,4 diamino- 5(3',4' dichlorophenyl)6 methylpyrimidine), 5,10-dideazatetrahydrofolate, 10-propargyl-5,8 dideazafolate (CB3717), 10-ethyl-10-deaza-aminopterin, deoxycytidine, 5-aza-cytosine arabinoside, N-4-palmitoyl-ara C, 2'-azido-2'-deoxy-ara C, N4-behenoyl-ara C, CCNU (lomustine), estramustine, MeCCNU, triethylene melamine, trenimon, dimethyl busulfan, streptozotocin, chlorozotocin, procarbazine, hexamethylmelamine (Altretamine), pentamethylmelamine (PMM), tetraplatin, oxaliplatin, platinum-DACH, aziridinybenzoquinone (AZQ), bleomycin, tallysomyacin S₁₀^b, liblomycin, pepleomycin, asparaginase (Elspar), pegaspargase (Oncaspar), Cladribine (leustatin), porfimer sodium (Photofrin), amonofide, deoxyspergualin, dihydrolenperone, flavone acetic acid, gallium nitrate, or hexamethylene bisacetamine (HMBA).

20. A method for determining a therapeutically effective amount of suramin for administering to a patient, who is to receive a cytotoxic agent, which comprises the steps of:

constructing a nomogram based on the following equations:

$$\text{First cycle dose (mg)} = \frac{(21.4 * 5.13 * \text{BSA}^2)}{e^{-(0.0026 \text{ or } 0.0022 * 48)}} = \text{FACTOR} * \text{BSA}^2 \quad \text{Eq. 15,}$$

and

$$\text{Subsequent cycle dose} = \text{First dose} * (1 - e^{-k * t}) = 125 * \text{BSA}^2 * (1 - e^{-k * t}) \quad \text{Eq. 16.}$$

21. The method of claim 20, wherein said nomogram is:

Nomogram For Calculating Suramin Dose

| | FACTOR | |
|--|--------|-------|
| | Man | Woman |
| Cycle 1* | 125 | 125 |
| Days since the administration of the first dose of previous cycle | FACTOR | |
| 7 | 39 | 33 |
| 8 | 43 | 37 |
| 9 | 47 | 40 |
| 10 | 51 | 44 |
| 11 | 55 | 47 |
| 12 | 58 | 50 |
| 13 | 61 | 53 |
| 14 | 64 | 56 |
| 15 | 67 | 58 |
| 16 | 70 | 61 |
| 17 | 72 | 63 |
| 18 | 74 | 66 |
| 19 | 77 | 68 |
| 20 | 79 | 70 |
| 21 | 80 | 72 |
| 22 | 82 | 74 |
| 23 | 84 | 75 |
| 24 | 86 | 77 |
| 25 | 87 | 79 |
| 26 | 88 | 80 |
| 27 | 90 | 82 |
| 28 | 91 | 83 |
| 29 | 92 | 84 |
| 30 | 93 | 86 |
| 31 | 94 | 87 |
| 32 | 95 | 88 |
| 33 | 96 | 89 |
| 34 | 97 | 90 |
| 35 | 98 | 91 |
| 36 | 98 | 92 |
| 37 | 99 | 93 |
| 38 | 100 | 94 |
| 39 | 100 | 95 |
| 41 | 102 | 96 |
| 42 | 102 | 97 |
| 44 | 103 | 98 |
| 47 | 104 | 100 |

| | | |
|----|-----|-----|
| 49 | 105 | 101 |
| 52 | 106 | 102 |
| 55 | 106 | 103 |

22. A kit for carrying out the combined administration of suramin with one or more cytotoxic agents, comprising:

- 5 (a) suramin formulated in a pharmaceutical carrier; and
- (b) instructions for therapeutic use of said suramin in combination with said cytotoxic agent(s) in one or more of inhibiting growth, proliferation of tumor cells, or inducing killing of tumor cells, calling for:
 - 10 (i) administering suramin, if required, in a required dose to establish a low circulating concentration of suramin in said patient of below about 200 μ M; and
 - (ii) administering said chemotherapeutic agent to said patient when said low circulating concentration of suramin of below about 200 μ M is present in said patient.

15 23. The kit of claim 22, wherein said instructions include a method for determining a therapeutically effective amount of suramin.

20 24. The kit of claim 23, wherein the instructions for determining a therapeutically effective amount of suramin comprise a nomogram.

25. The kit of claim 22, wherein one of the cytotoxic agents is paclitaxel.

26. The kit of claim 22, wherein one of the cytotoxic agents is carboplatin.